Pilot Randomised Controlled Trial to Test Effectiveness of Facemasks in Preventing Influenza-like Illness Transmission among Australian Hajj Pilgrims in 2011

Article · March 2014

DOI: 10.2174/1871526514666141021112855

CITATIONS
49

READS
1,386

37 authors, including:

Osamah Barasheed
King Abdullah Medical City
36 PUBLICATIONS **485** CITATIONS
SEE PROFILE

Al-Mamoon Badahdah
The University of Sydney
19 PUBLICATIONS **128** CITATIONS
SEE PROFILE

Leon Heron
The New South Wales Department of Health
76 PUBLICATIONS **1,688** CITATIONS
SEE PROFILE

Janette Taylor
The University of Sydney
32 PUBLICATIONS **831** CITATIONS
SEE PROFILE

Pilot Randomised Controlled Trial to Test Effectiveness of Facemasks in Preventing Influenza-like Illness Transmission among Australian Hajj Pilgrims in 2011

Osamah Barasheed[1*], Nedal Almasri[2], Al-Mamoon Badahdah[3], Leon Heron[1], Janette Taylor[4], Kenneth McPhee[4], Iman Ridda[1], Elizabeth Haworth[5], Dominic E Dwyer[4,6,7], Harunor Rashid[1,7] and Robert Booy[1,6,7] on behalf of the Hajj Research Team[**]

[1]National Centre for Immunisation Research and Surveillance (NCIRS), The Children's Hospital at Westmead, NSW, Australia; [2]Ministry of Health, Jeddah, Saudi Arabia; [3]Department of Family and Community Medicine, Faculty of Medicine, King Abdulaziz University, Rabigh, Saudi Arabia; [4]Centre for Infectious Diseases and Microbiology Laboratory Services, Westmead Hospital, NSW, Australia; [5]Menzies Research Institute Tasmania, Hobart, Tasmania, Australia; [6]Marie Bashir Institute for Infectious Diseases and Biosecurity, School of Biological Sciences and Sydney Medical School, University of Sydney, Australia; [7]Sydney Medical School, The University of Sydney, NSW, Australia

Abstract: Studies to determine the effectiveness of facemasks in preventing influenza have been inconclusive, largely due to small sample size. The Hajj pilgrimage, where the incidence of influenza and other respiratory infections is high, provides an excellent opportunity to test the effectiveness of facemasks against syndromic and laboratory-confirmed infections. Hence, a pilot study was conducted among Australian pilgrims to assess the feasibility of such a large-scale trial in the coming years. At the 2011 Hajj, tents were randomised to 'supervised mask use' versus 'no supervised mask use'. Pilgrims with ILI symptoms for ≤3 days were recruited as 'cases' and those who slept within 2 meters of them as 'contacts'. Surgical facemasks were provided to cases and contacts in the 'mask' tents, but not in the 'control' tents. Pilgrims in both groups were given diaries to record their respiratory symptoms. Nasal or pharyngeal swabs were collected from the cases and contacts with ILI for point-of-care and nucleic acid tests. A total of 22 tents were randomised to 'mask' (n=12) or 'control' (n=10). There were 164 pilgrims recruited; 75 in 'mask' and 89 in 'control' group. Mask use compliance was 76% in the 'mask' group and 12% in the 'control' group. Based on developing syndromic ILI, less contacts became symptomatic in the 'mask' tents compared to the 'control' tents (31% versus 53%, p= 0.04). However, laboratory results did not show any difference between the two groups. This pilot study shows that a large trial to assess the effectiveness of facemasks use at Hajj is feasible.

Keywords: Facemask, Hajj, influenza-like illness, Mecca, pilgrims, respiratory infections.

INTRODUCTION

Up to three million pilgrims from all over the world, including about 4000-4500 from Australia, travel to Saudi Arabia for Hajj every year. All pilgrims spend five days of the Hajj month (called *Dulhijjah*) in designated places in Mecca, specifically Mina, Arafat and Muzdalifa, living in pre-determined groups in selected tents, as well as one night in the open. About 50-100 pilgrims occupy each large tent, allocated by gender and country of origin. The intense crowding, reduced access to hygiene and environmental stress facilitates the spread of infections including meningococcal disease, influenza and pneumonia [1-8]. Influenza-like illness (ILI) is the most common medical presentation to primary care, and pneumonia is the leading cause of hospital admission during Hajj [4-8]. Guidelines on how to minimise health hazards at Hajj and other mass gatherings have been published annually by the Saudi Arabian Ministry of Health [9].

A recent study based on observation of photo frames during the 2009 (pandemic year) and 2013 Hajj revealed that overall 8.4% and 0.02% pilgrims respectively used facemasks [10]. The role of facemasks in the prevention of spread of ILI, in Hajj and other settings, is not clear with results from previous studies being either conflicting or inconclusive [11-21]. For instance, a randomised controlled trial (RCT) found that facemasks used in a household setting decreased the risk of ILI [12], while, by contrast, a case-control study among health care workers (HCWs) at Hajj showed, surprisingly, that intermittent use of facemask was associated with a 2.7 fold greater risk of infection. The authors attributed this to contamination of facemasks with infectious respiratory secretions [22]. Meta-analysis of five trials showed that wearing facemasks appears to be protec-

*Address correspondence to this author at the National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead, Cnr Hawkesbury Rd and Hainsworth St, Locked Bag 4001, Westmead NSW 2145, Australia; Tel: +61 431 103 101; Fax: +61 2 9845 1418;
E-mail: osamah.barasheed@health.nsw.gov.au

**[Jassir Alshehri, Mukhtaar Als, Hamid Bokhary, Yahya Alghamdi, Daliya Alansari, Amani AL-Hetairshi, Maria Chow, Duaa Sakabumi, Samah Melebari, Nada Dibi, Nadeen Kalantan, Amani AL-Beladi, Duaa Tashkandi, Wadha AL-Otaiby, Reham Abu Zahirah, Samah Alhadramy, Ziyad Siyam, Mohamad Bakhaidar, Ahmad Basalamah, Suhaib Jiman, Abdullah Alotaibi, Musab Hijan, Saeed Abuzidbarabwan, Mousab AL-Sudais, Saad Alghamdi, Saeed Alghamdi and Mohamud Sheikh].

2212-3989/14 $58.00+.00

tive against ILI, but not against laboratory-confirmed influenza [23]. These findings accord with those from other systematic reviews [11, 13]. The major limitation of previous studies was small sample size, lacking the power to detect effects of facemasks on laboratory-confirmed influenza or other infections [11, 23]. Researchers recommended larger trials with sufficient power to have conclusive results [11].

Conducting a trial at Hajj pilgrimage offers an excellent opportunity to do research in a semi-closed setting.

We conducted a pilot study during the Hajj in 2011 to explore the feasibility of establishing a large-scale trial to test the effectiveness of facemasks in preventing respiratory virus infections among Hajj pilgrims to better inform policy makers, religious jurists and other stakeholders.

METHODS

During the 2011 Hajj pilgrimage, we conducted a pilot study of a non-blinded cluster randomised trial of 'supervised mask use' versus 'no supervised mask use' among pilgrims who developed symptoms of ILI during the Hajj week (4-10 November 2011) in Mina, Saudi Arabia. Participants were Australian pilgrims aged ≥ 15 years who attended the 2011 Hajj. ILI was defined as subjective (or proven) fever plus one respiratory symptom (e.g. dry or productive cough, runny nose, sore throat, shortness of breath). Those reporting new onset of ILI were designated as 'cases'. Also we enrolled 'contacts' i.e. pilgrims who shared the same tent and slept in an adjacent bed within 2 meters to 'cases' (Fig. **1** and **2**).

Randomisation and Intervention

Study brochures were distributed to Australian pilgrims in Mosques, Islamic Centres and pre-travel seminars in Australia and during their stay in hotels in Mecca, Saudi Arabia before they travelled to their tents in the Mina valley, located at the outskirts of Mecca.

The tent was the randomisation unit, and tents were randomised to either intervention group (supervised mask tent) or control group (no supervised mask tent) by an independent study coordinator who was not an investigator. For the intervention group, we used a plain surgical facemask (3M™ Standard Tie-On Surgical Mask, Cat No: 1816) manufactured by 3M company, USA, that we purchased from a wholesaler in Saudi Arabia.

Australian pilgrims who had ILI symptoms for 3 days or less were invited to participate as a 'case'. People who slept in an adjacent bed were invited to participate as a 'contact'. Following further verbal explanation, informed consent was obtained in writing from all participants. Adults aged ≥ 18 years consented for themselves while for children aged < 18 years, consent was obtained from their parent or legal guardian.

For intervention tent groups, masks were provided to both index cases and their contacts. Advice on mask use was given throughout their stay in Mina: before prayers, in seminars and after meals. Written instructions were provided on how to use facemasks, when to change them and when (i.e. if damp or damaged) and where (a special polythene bag) to discard used masks.

Pilgrims allocated to control tents were not provided with facemasks but general information on hygiene was given to them. Participants in both tent groups were provided with diaries to write down any new or continuing symptoms over the 5 day study period.

Participants were examined by Muslim doctors at Hajj with support from trained research nurses and public health staff.

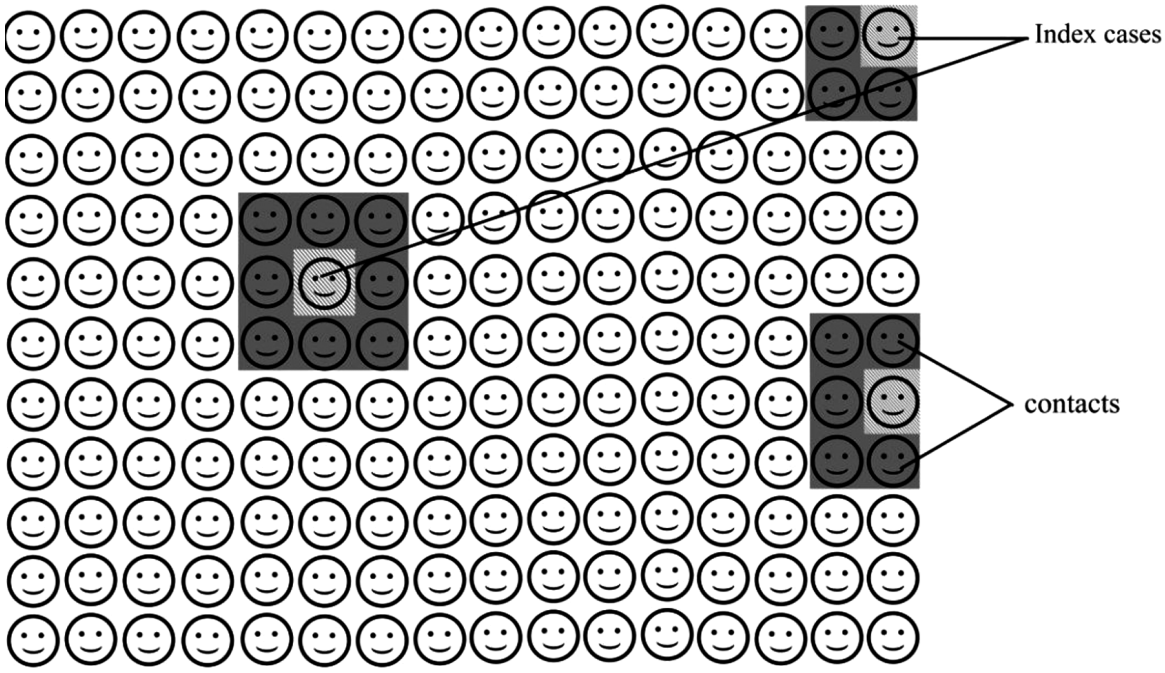

Fig. (1). Schematic representation of 'cases' (light grey) and 'contacts' (dark grey) in a tent of Australian Hajj pilgrims in 2011.

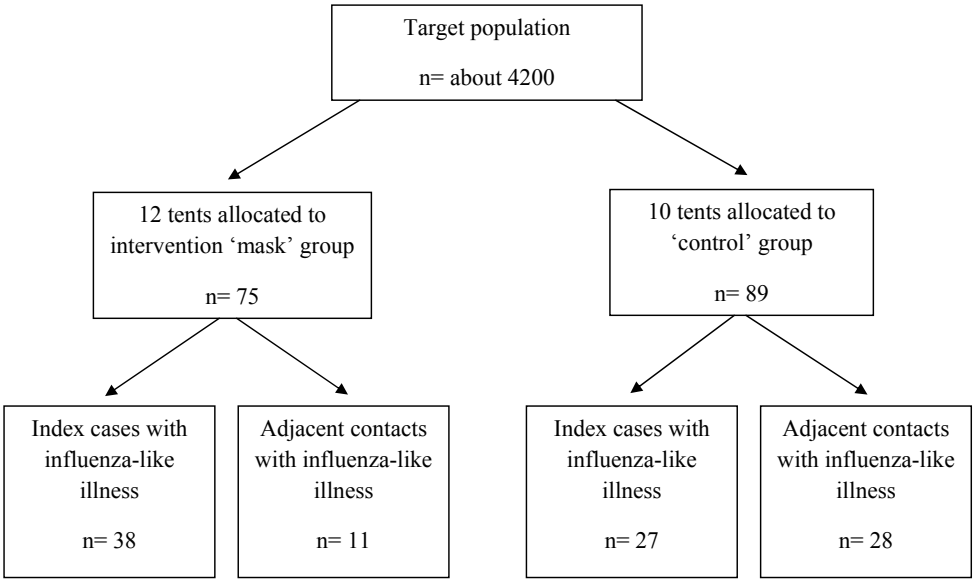

Fig. (2). Flow diagram showing recruitment of participants during Hajj in 2011.

Because advice from the Saudi Ministry of Hajj to all pilgrims included recommending the wearing of masks, all pilgrims, both cases and controls, were asked about mask wearing [24].

Two nasal swabs, one from each nostril, were taken from each case of ILI by trained collectors at the time of recruitment and from all symptomatic contacts within 2-3 days of symptom onset. One swab was used for influenza point of care testing (POCT) using the QuickVue Influenza (A+B) assay (Quidel Corporation, San Diego, USA), and the other was immersed in universal viral transport media for later nucleic acid testing (NAT) [25]. The latter was stored within 6-8 hours in a cooler box at 4°C temperature then transported by the end of the day to the microbiology laboratory of the Custodian of the two Holy Mosques Institute for Hajj and Umrah Research, Mecca. After the Hajj season, all samples were shipped to the Centre for Infectious Disease and Microbiology Laboratory Services, Westmead Hospital, Sydney, Australia. Participants showing positive result for influenza by POCT were offered oseltamivir if the duration of illness was less than 3 days.

Follow Up

Subjects reporting ILI symptoms and their close tent contacts were followed for up to 5 days from the date of recruitment into the study using their diary and text message/telephonic reminders. They were reminded by phone and/or email to return their completed diaries after Hajj with clear information on the progress of their ILI. Any outstanding queries were thereby resolved.

Measuring Instruments

The outcomes of the trial were measured using a) questionnaires, b) symptom diaries, and c) results of testing on nasal swabs. The latter was based on both POCT by QuickVue A+B Influenza test and NAT for influenza and other respiratory viruses. Analysis of ILI symptom reports in questionnaires and diaries and presence of test-confirmed influenza or other viruses allowed comparison of 'intervention' and 'control' groups to assess the effectiveness of mask use.

Data Analysis and Interpretation

Data were compiled into a Microsoft Excel 2010 spread sheet. Analysis was performed using the Statistical Package for the Social Sciences (SPSS® 19, Chicago, IL, USA). Data were analysed descriptively. Categorical variables were compared by using the Chi-square test and continuous data by the Student's t test. A p value of ≤ 0.05 was considered statistically significant.

Ethics Approval

The study was approved by the Institutional Review Board of King Fahd Medical City, Ministry of Health, Riyadh, Saudi Arabia (Ref: KACST: H-01-R-012) and by the Human Research Ethics Committee (HREC) at Sydney Children's Hospital Network, Australia (Ref: 11/SCHN/162). In addition, this study has been registered at the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12613001007729.

RESULTS

Twenty two tents were randomly selected from the Australian pilgrims camped in Mina, during Hajj in 2011; 12 tents were allocated to the 'mask' group and 10 tents to the 'control' group. A total of 164 pilgrims were recruited; 75 in the 'mask' group (39 'cases' and 36 'contacts'), and 89 in the 'control' group (36 'cases' and 53 'contacts'). All pilgrims in both groups were followed up during the peak period of the 2011 Hajj (Fig. **2**).

Participants were cooperative; all but one pilgrim returned their diaries and no one dropped out or were excluded from the study. However we faced some logistic challenges: for instance, there was a delay in realeasing POCT kits from

customs which was ultimately resolved by revised documentation. Demographic data are presented in Table **1**. There were significant differences in gender (more males in 'control' group) and ethnicities (more Middle eastern pilgrims in 'mask' group) between the groups.

Compliance with facemask use by pilgrims in the 'mask' group was 56 of 75 (76%), while it was 11 of 89 (12%) in the 'control' group ($p<0.001$). The proportion of facemask user in the 'mask' tents was 76% for both males (19/25) and females (38/50). The most often reported reason for not wearing facemasks was discomfort (15%).

The duration of mask use varied among pilgrims in 'mask' tents. Pilgrims who used facemasks for > 8 hours per day experienced a lower rate of ILI than those who used them for ≤ 8 hours (Table **2**). Only 10 of 75 (13%) pilgrims in 'mask' tents wore facemasks during sleep.

The most common respiratory symptoms reported were cough (n= 76), sore throat (n= 57) and runny nose (n= 38). Other symptoms are shown in Fig. **3**. Thirty one percent (11/36) of contacts in 'mask' tents compared with 53% (28/53) contacts in 'control' tents reported ILI consistent with our case definition (p= 0.04).

By POCT, two samples were positive for influenza. Both were negative for influenza, though one was positive for rhinovirus by NAT.

Of the 80 swabs, collected, NAT showed that 18 index cases in the 'mask' tents had viral infections (14 rhinovirus, 3 influenza [2 A and 1 B] and 1 parainfluenza virus 3) and 23 index cases in 'control' tents (18 rhinovirus, 3 influenza [2 A and 1 B], 1 enterovirus and 1 dual infection of rhinovirus and influenza A). However, only 4 contacts in the 'mask' group had NAT-confirmed viral infections (3 rhinoviruses and 1 dual infection of rhinovirus and influenza B) compared with only 2 in 'control' group, both rhinoviruses (Table **3**).

DISCUSSION

This pilot study showed that a trial to assess the effectiveness of facemasks against respiratory viral infections is feasible and can be conducted during Hajj pilgrimage. Although pilgrims were busy with their Hajj rituals and prayers, they were both cooperative and motivated to participate in such a trial. The facemask compliance among Australian pilgrims in the 'mask' group of 76% was much higher than that reported for pilgrims in general during the influ-

Table 1. Demography of 164 Australian Hajj pilgrims in 2011 by study group.

Categories	Mask	Control	P value
Number of participants	75	89	
Median age in years (range)	48 (19-80)	41.6 (17-72)	0.7
Gender			
Male: female	25:50	46:43	0.02
At risk (≥65 or had chronic disease)	20 (27%)	16 (18%)	0.2
Smoker	12 (16%)	7 (8%)	0.1
Ethnicity			
South and South East Asian	26 (35%)	36 (40%)	0.4
Middle eastern (including Lebanese)	29 (38%)	12 (14%)	0.001
Others	20 (27%)	41 (46%)	0.01
Some or all of roommate had ILI	51 (68%)	52 (58.4%)	0.2
'Contacts' developed ILI symptoms	11/36 (31%)	28/53 (53%)	0.04

Table 2. The relationship between duration of using facemasks and developing symptoms of influenza-like illness (ILI) among 'contacts' at 'mask' tents of Australian Hajj pilgrims in 2011 (n= 36)*.

Duration of mask wearing by hours	Had ILI symptoms	No ILI symptoms	P value
No mask	5/35 (14.3%)	2/35 (5.7%)	0.2
≤ 4	7/35 (20%)	4/35 (11.4%)	0.3
5-8	3/35 (8.6%)	5/35 (14.3%)	0.4
>8	1/35 (2.9%)	8/35 (22.9%)	0.01

*1 pilgrim did not return his diary.

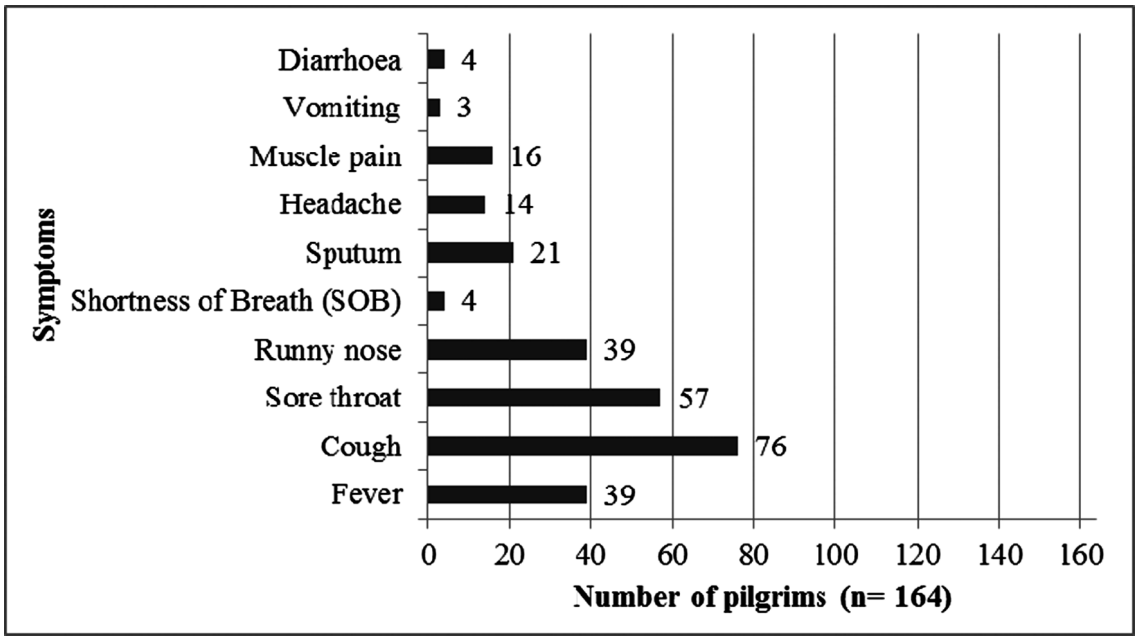

Fig. (3). Clinical symptoms developed by Australian Hajj pilgrims during Hajj in 2011 (n= 164).

Table 3. Virology results of Australian pilgrims who developed respiratory symptoms and swabbed during Hajj in 2011 (n= 80).

Virology results	Mask group	Control group	P value
'Index cases':	**n= 39**	**n= 35**	
Rhinovirus	14 (36%)	18 (51%)	0.2
Influenza A	2 (5%)	2 (6%)	0.9
Influenza B	1 (3%)	1 (3%)	0.9
Dual infection (rhino & influenza A)	-	1 (3%)	0.3
Parainfluenza 3	1 (3%)	-	0.3
Enterovirus	-	1 (3%)	0.3
'Contacts':	**n= 4**	**n= 2**	
Rhinovirus	3 (75%)	2 (100%)	0.4
Influenza	-	-	-
Dual infection (rhino & influenza B)	1 (25%)	-	0.4
Parainfluenza	-	-	-
Enterovirus	-	-	-

influenza pandemic year 2009 (8%) and in 2013 (0.02%) as assessed in a photographic frame study [10]. This implies that pilgrims would comply with mask use if clearly recommended and the purpose explained. Additionally, 12% pilgrims in the 'control' group used facemasks, which is similar to the baseline rate of mask use in 2009 but higher than that of 2013 [10].

Facemask use reported by Hajj pilgrims varies by study years and the country of origin of the pilgrims. For instance, 56% Saudi Arabian, 42% US, and 79% French pilgrims used facemasks in 2009 while 73% Malaysian pilgrims used them in 2007 [26-29]. Similar variation was observed across five countries in four continents in a large-scale polling study conducted among nationally representative sample of adults during the 2009 pandemic year [30].

Although the sample size of this pilot study was small, it indicated that wearing facemasks appeared to be protective against syndromic ILI when compared to controls (31% versus 53%, p= 0.04). This concurs with most other studies as well as the meta-analysis conducted by Rashid *et al.* [12-16, 23].

In our study, we measured the pilgrims' daily compliance with facemasks by quantified duration of use. Previous randomised controlled trials that assessed the effectiveness of facemasks in preventing ILI in households used less quantitative descriptive terms such as, "always", "mostly", "sometimes" or "never" to indicate the duration of facemask use

[12-21]. However, Canini and colleagues attempted to evaluate the relationship between the duration of facemask use and protection against ILI among households in France during the 2008-2009 influenza season but omitted secondary ILIs among households [17]. Our study has demonstrated a positive association between the duration of facemask use and protection against ILI. For instance, only 3% of pilgrims who used facemasks for more than eight hours developed ILI while 43% of those who used masks for eight hours or less reported ILI ($p< 0.001$). Although the distribution of gender and ethnicity was different for 'mask' and 'control' groups, the effect of facemask in reducing the transmission of ILI was similar across the genders and ethnicities. As in previous studies, the main reason given for not wearing facemasks was discomfort, especially at night during sleep.

In this study, almost half (46%) of the participants complained of cough, about a third (35%) of sore throat and about one fourth (24%) reported rhinorrhoea or fever. These are similar to the frequency of respiratory symptoms in French pilgrims during Hajj 2009: 48.5% complained of cough, 36.1% sore throat and 23.7% had rhinorrhoea [28]. Cough was also the commonest symptom among Malaysian Hajj pilgrims in 2007, but it was higher than in our study (91.5% versus 46%) [29].

The point-prevalence of ILI among 'contacts' in our study was 44% (39/89), most of them from 'control' tents (28 out of 39). This prevalence of ILI was higher than among Australian pilgrims during subsequent Hajj seasons 2012 (9%) [31] and 2013 (11%) [Dr Barasheed, Sydney, personal communication] but nearly similar to that of the Malaysian pilgrims in 2007 (40%) [29] and French pilgrims during the Hajj 2013 (47%) as well as 2012 (41%) [28, 32, 33]. However, it was lower than the Malaysians in 2013 (86%) [Dr Habsah Hasan, Kelantan, Malaysia, personal communication on 12th May 2014]. These differences might be explained by varying methodology and sample size or demographic differences such as age, the prevalence of underlying chronic diseases, and/or seasonal and geographic variations in respiratory virus circulation. Australian pilgrims' tents are usually smaller and less crowded than for pilgrims from other countries, which might reduce transmission of ILI.

Although nasal swabs for laboratory-confirmation were few and inconclusive, they indicated that rhinoviruses were the commonest virus detected, consistent with previous findings at Hajj [6, 34-36].

We believe that this study was the first randomised controlled trial of a preventive intervention among Hajj pilgrims in which, for the five peak Hajj days, pilgrims were closely followed and monitored by a trained medical team. However, this was a pilot study with small sample, which has shown the feasibility of a future full-scale study but yielded no conclusive findings.

In summary, this pilot study shows that a trial to assess the effectiveness of facemasks during a mass gathering such as Hajj is warranted and now being undertaken. Although we faced logistic challenges, these can be reduced by effective collaboration and early preparation. We liaised with collaborators from a number of countries, secured a competitive research grant from Qatar National Research Fund (QNRF) and commenced our definitive trial in 2013. Its findings should provide the evidence needed.

CONFLICT OF INTEREST

Leon Heron and Robert Booy have received funding from Baxter, CSL, GSK, Merck, Novartis, Pfizer, Roche, and Sanofi Pasteur for the conduct of sponsored research, travel to present at conferences or consultancy work; all funding received is directed to research accounts at the Children's Hospital at Westmead. The other authors have declared no conflict of interest in relation to this work.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the help and the support of: the Royal Embassy of Saudi Arabia, Canberra; Saudi Arabian Cultural Mission, Canberra; Ministry of Higher Education, Riyadh; Ministry of Hajj (Deputy Minister's Office), Mecca; the Custodian of the two Holy Mosques Institute for Hajj and Umrah Research (Dr. Abdulaziz Seroji and Dr. Atif Asghar), Mecca; Islamic Medical Association at Kingdom of Saudi Arabia (IMAKSA) and the World Assembly of Muslim Youth (WAMY), Mecca; Mr. Mohammad Barashid, Sydney; Mr. Ahmad Barshaid and Ms. Aisha Barshaid, Yanbu.

This study is registered at Australian New Zealand Clinical Trials Registry (ANZCTR), ACTRN: ACTRN12613001007729 (http://www.anzctr.org.au).

REFERENCES

[1] El Bashir, H.; Coen, P. G.; Haworth, E.; Taylor, S.; Mifsud, A.; El Baki, A.; Zuckerman, J.; Gray, S. J.; Booy, R. Meningococcal W135 carriage; enhanced surveillance amongst east London Muslim pilgrims and their household contacts before and after attending the 2002 Hajj. *Travel Med. Infect. Dis*., **2004**, *2*(1), 13-5.

[2] Aguilera, J. F.; Perrocheau, A.; Meffre, C.; Hahne, S.; Group, W. W. Outbreak of serogroup W135 meningococcal disease after the Hajj pilgrimage, Europe, 2000. *Emerg. Infect. Dis*., **2002**, *8*(8), 761-7.

[3] Moore, P. S.; Reeves, M. W.; Schwartz, B.; Gellin, B. G.; Broome, C. V. Intercontinental spread of an epidemic group A Neisseria meningitidis strain. *Lancet,* **1989**, *2*(8657), 260-3.

[4] Haworth, E.; Barasheed, O.; Memish, Z. A.; Rashid, H.; Booy, R. Prevention of influenza at Hajj: applications for mass gatherings. *J. R. Soc. Med*., **2013**, *106*(6), 215-23.

[5] Rashid, H.; Shafi, S.; Booy, R.; El Bashir, H.; Ali, K.; Zambon, M.; Memish, Z.; Ellis, J.; Coen, P.; Haworth, E. Influenza and respiratory syncytial virus infections in British Hajj pilgrims. *Emerg. Health Threats J.,* **2008**, *1*, e2.

[6] Rashid, H.; Shafi, S.; Haworth, E.; El Bashir, H.; Memish, Z. A.; Sudhanva, M.; Smith, M.; Auburn, H.; Booy, R. Viral respiratory infections at the Hajj: comparison between UK and Saudi pilgrims. *Clin. Microbiol. Infect.*, **2008**, *14*(6), 569-74

[7] Asghar, A. H.; Ashshi, A. M.; Azhar, E. I.; Bukhari, S. Z.; Zafar, T. A.; Momenah, A. M. Profile of bacterial pneumonia during Hajj. *Indian J. Med. Res*., **2011**, *133*, 510-3.

[8] Rashid, H.; Abdul Muttalif, A. R.; Mohamed Dahlan, Z. B.; Djauzi, S.; Iqbal, Z.; Karim, H. M.; Naeem, S. M.; Tantawichien, T.; Zotomayor, R.; Patil, S.; Schmitt, H. J. The potential for pneumococcal vaccination in Hajj pilgrims: expert opinion. *Travel Med. Infect. Dis*., **2013**, *11*(5), 288-94.

[9] Memish, Z. A.; Al Rabeeah, A. A. Health conditions for travellers to Saudi Arabia for the Umra and pilgrimage to Mecca (Hajj) - 2014. *J. Epidemiol. Glob. Health*, **2014**, *4*(2), 73-5.

[10] Elachola, H.; Assiri, A. M.; Memish, Z. A. Mass gathering-related mask use during 2009 pandemic influenza A (H1N1) and Middle East respiratory syndrome coronavirus. *Int. J. Infect. Dis*., **2014**, *20*, 77-8.

[11] Bin-Reza, F.; Lopez Chavarrias, V.; Nicoll, A.; Chamberland, M. E. The use of masks and respirators to prevent transmission of influenza: a systematic review of the scientific evidence. *Influenza Other Respir. Viruses,* **2012**, *6*(4), 257-67.

[12] MacIntyre, C. R.; Cauchemez, S.; Dwyer, D. E.; Seale, H.; Cheung, P.; Browne, G.; Fasher, M.; Wood, J.; Gao, Z.; Booy, R.; Ferguson, N. Face mask use and control of respiratory virus transmission in households. *Emerg. Infect. Dis.*, **2009**, *15*(2), 233-41.

[13] Cowling, B. J.; Chan, K. H.; Fang, V. J.; Cheng, C. K.; Fung, R. O.; Wai, W.; Sin, J.; Seto, W. H.; Yung, R.; Chu, D. W.; Chiu, B. C.; Lee, P. W.; Chiu, M. C.; Lee, H. C.; Uyeki, T. M.; Houck, P. M.; Peiris, J. S.; Leung, G. M. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. *Ann. Intern. Med.*, **2009**, *151*(7), 437-46.

[14] Suess, T.; Remschmidt, C.; Schink, S. B.; Schweiger, B.; Nitsche, A.; Schroeder, K.; Doellinger, J.; Milde, J.; Haas, W.; Koehler, I.; Krause, G.; Buchholz, U. The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009-2011. *BMC Infect. Dis.*, **2012**, *12*, 26.

[15] Aiello, A. E.; Murray, G. F.; Perez, V.; Coulborn, R. M.; Davis, B. M.; Uddin, M.; Shay, D. K.; Waterman, S. H.; Monto, A. S. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. *J. Infect. Dis.*, **2010**, *201*(4), 491-8.

[16] Larson, E. L.; Ferng, Y. H.; Wong-McLoughlin, J.; Wang, S.; Haber, M.; Morse, S. S. Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households. *Public Health Rep.*, **2010**, *125*(2), 178-91.

[17] Canini, L.; Andreoletti, L.; Ferrari, P.; D'Angelo, R.; Blanchon, T.; Lemaitre, M.; Filleul, L.; Ferry, J. P.; Desmaizieres, M.; Smadja, S.; Valleron, A. J.; Carrat, F. Surgical mask to prevent influenza transmission in households: a cluster randomized trial. *PLoS One,* **2010**, *5*(11), e13998.

[18] Simmerman, J. M.; Suntarattiwong, P.; Levy, J.; Jarman, R. G.; Kaewchana, S.; Gibbons, R. V.; Cowling, B. J.; Sanasuttipun, W.; Maloney, S. A.; Uyeki, T. M.; Kamimoto, L.; Chotipitayasunondh, T. Findings from a household randomized controlled trial of hand washing and face masks to reduce influenza transmission in Bangkok, Thailand. *Influenza Other Respir. Viruses,* **2011**, *5*(4), 256-67.

[19] Loeb, M.; Dafoe, N.; Mahony, J.; John, M.; Sarabia, A.; Glavin, V.; Webby, R.; Smieja, M.; Earn, D. J.; Chong, S.; Webb, A.; Walter, S. D. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA,* **2009**, *302*(17), 1865-71.

[20] MacIntyre, C. R.; Wang, Q.; Cauchemez, S.; Seale, H.; Dwyer, D. E.; Yang, P.; Shi, W.; Gao, Z.; Pang, X.; Zhang, Y.; Wang, X.; Duan, W.; Rahman, B.; Ferguson, N. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir. Viruses,* **2011**, *5*(3), 170-9.

[21] MacIntyre, C. R.; Wang, Q.; Seale, H.; Yang, P.; Shi, W.; Gao, Z.; Rahman, B.; Zhang, Y.; Wang, X.; Newall, A. T.; Heywood, A.; Dwyer, D. E. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am. J. Respir. Crit. Care Med.*, **2013**, *187*(9), 960-6.

[22] Al-Asmary, S.; Al-Shehri, A. S.; Abou-Zeid, A.; Abdel-Fattah, M.; Hifnawy, T.; El-Said, T. Acute respiratory tract infections among Hajj medical mission personnel, Saudi Arabia. *Int. J. Infect. Dis.*, **2007**, *11*(3), 268-72.

[23] Rashid, H.; Booy, R.; Heron, L.; Memish, Z. A.; Nguyen-Van-Tam, J.; Barasheed, O.; Haworth, E. Unmasking masks in Makkah: preventing influenza at Hajj. *Clin. Infect. Dis.*, **2012**, *54*(1), 151-3.

[24] Ministry of Health. Health Regulations for Travellers to KSA for Hajj. Riyadh, Saudi Arabia: Ministry of Health; 2011. Available from: http://www.moh.gov.sa/en/HealthAwareness/Hajj/Pages/default.aspx (Accessed May 15, **2014**).

[25] Playford, E. G.; Dwyer, D. E. Laboratory diagnosis of influenza virus infection. *Pathology*, **2002**, *34*(2), 115-25.

[26] Al-Jasser, F. S.; Kabbash, I. A.; Almazroa, M. A.; Memish, Z. A. Patterns of diseases and preventive measures among domestic hajjis from Central, Saudi Arabia. *Saudi Med. J.*, **2012**, *33*(8), 879-86.

[27] Balaban, V.; Stauffer, W. M.; Hammad, A.; Afgarshe, M.; Abd-Alla, M.; Ahmed, Q.; Memish, Z. A.; Saba, J.; Harton, E.; Palumbo, G.; Marano, N. Protective practices and respiratory illness among US travelers to the 2009 Hajj. *J. Travel Med.*, **2012**, *19*(3), 163-8.

[28] Gautret, P.; Vu Hai, V.; Sani, S.; Doutchi, M.; Parola, P.; Brouqui, P. Protective measures against acute respiratory symptoms in French pilgrims participating in the Hajj of 2009. *J. Travel Med.*, **2011**, *18*(1), 53-5.

[29] Deris, Z. Z.; Hasan, H.; Sulaiman, S. A.; Wahab, M. S.; Naing, N. N.; Othman, N. H. The prevalence of acute respiratory symptoms and role of protective measures among Malaysian hajj pilgrims. *J. Travel Med.*, **2010**, *17*(2), 82-8.

[30] SteelFisher, G. K.; Blendon, R. J.; Ward, J. R.; Rapoport, R.; Kahn, E. B.; Kohl, K. S. Public response to the 2009 influenza A H1N1 pandemic: a polling study in five countries. *Lancet Infect. Dis.*, **2012**, *12*(11), 845-50.

[31] Rashid, H.; Barasheed, O.; Booy, R. Acute febrile respiratory infection symptoms in Australian Hajjis at risk of exposure to Middle East respiratory syndrome coronavirus. *Med. J. Aust.*, **2013**, *199*(7), 453.

[32] Gautret, P.; Charrel, R.; Benkouiten, S.; Belhouchat, K.; Nougairede, A.; Drali, T.; Salez, N.; Memish, Z. A.; Al Masri, M.; Lagier, J. C.; Million, M.; Raoult, D.; Brouqui, P.; Parola, P. Lack of MERS coronavirus but prevalence of influenza virus in French pilgrims after 2013 Hajj. *Emerg. Infect. Dis.*, **2014**, *20*(4), 728-30.

[33] Gautret, P.; Charrel, R.; Belhouchat, K.; Drali, T.; Benkouiten, S.; Nougairede, A.; Zandotti, C.; Memish, Z. A.; al Masri, M.; Gaillard, C.; Brouqui, P.; Parola, P. Lack of nasal carriage of novel corona virus (HCoV-EMC) in French Hajj pilgrims returning from the Hajj 2012, despite a high rate of respiratory symptoms. *Clin. Microbiol. Infect.*, **2013**, *19*(7), E315-317.

[34] Benkouiten, S.; Charrel, R.; Belhouchat, K.; Drali, T.; Salez, N.; Nougairede, A.; Zandotti, C.; Memish, Z. A.; al Masri, M.; Gaillard, C.; Parola, P.; Brouqui, P.; Gautret, P. Circulation of respiratory viruses among pilgrims during the 2012 Hajj pilgrimage. *Clin. Infect. Dis.*, **2013**, *57*(7), 992-1000.

[35] Memish, Z. A.; Assiri, A. M.; Hussain, R.; Alomar, I.; Stephens, G. Detection of respiratory viruses among pilgrims in Saudi Arabia during the time of a declared influenza A(H1N1) pandemic. *J. Travel Med.*, **2012**, *19*(1), 15-21.

[36] Alborzi, A.; Aelami, M. H.; Ziyaeyan, M.; Jamalidoust, M.; Moeini, M.; Pourabbas, B.; Abbasian, A. Viral etiology of acute respiratory infections among Iranian Hajj pilgrims, 2006. *J. Travel Med.*, **2009**, *16*(4), 239-42.

Received: April 21, 2014 **Revised: June 25, 2014** **Accepted: June 27, 2014**